HED DOC. NO. 014676

September 19, 2001

MEMORANDUM

SUBJECT: ***PROPANIL*** - Report of the FQPA Safety Factor Committee.

FROM: Brenda Tarplee, Executive Secretary
FQPA Safety Factor Committee
Health Effects Division (7509C)

THROUGH: Ed Zager, Chair
FQPA Safety Factor Committee
Health Effects Division (7509C)

TO: Richard Griffin, Risk Assessor
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PC Code: 028201

The Health Effects Division (HED) FQPA Safety Factor Committee met on September 10, 2001 to evaluate the hazard and exposure data for propanil and recommended that the FQPA safety factor (as required by the Food Quality Protection Act of August 3, 1996) be retained at 10x in assessing the risk posed by this chemical.

I. HAZARD ASSESSMENT

(*Correspondence:* R. Griffin to B. Tarplee dated 09/06/01)

1. Adequacy of Toxicity Database

With the exception of the developmental neurotoxicity study, the toxicology data base for propanil is adequate for FQPA assessment. There are acceptable developmental toxicity studies in rats and rabbits and acceptable two-generation reproduction study in rats.

2. Determination of Susceptibility

There was no indication of increased susceptibility following *in utero* exposure to propanil in the prenatal developmental toxicity studies in rats and rabbits.

However, there was evidence consistent with neuro-endocrine disruption (delayed vaginal opening and preputial separation) in the 2-generation reproduction study which indicated a **qualitative susceptibility** to the offspring.(HED Doc. No. 014651).

3. Requirement of a Developmental Neurotoxicity Study

The HIARC concluded that a developmental neurotoxicity study with propanil is required due to suggestive evidence of neurotoxicity in the data base including neuropathological lesions (sciatic nerve degeneration) in a rat chronic/carcinogenicity study. There is also evidence consistent with neuro-endocrine disruption (delayed vaginal opening and preputial separation) in the two-generation reproduction study in rats, and in the rat chronic/carcinogenicity study (increased incidence of testicular interstitial cell tumors). This evidence is supported by the Structure Activity Relationship (SAR) consideration that linuron, which is structurally related to propanil, has a known neuro-endocrine mode of action.

II. EXPOSURE ASSESSMENT AND RISK CHARACTERIZATION

1. Dietary (Food) Exposure Considerations

(*Correspondence:* R. Griffin to B. Tarplee dated 09/06/01)

Propanil is a selective postemergence herbicide registered for use on barley, oats, rice, and wheat. Use on rice accounts for more than 99% of the total usage. The HED Metabolism Assessment Review Committee (MARC) concluded that the residue to be regulated in plants and animals is propanil and residues convertible to 3,4-dichloroaniline (3,4-DCA). The Agency has determined that there is a concern for secondary transfer of propanil residues of concern to meat, milk, poultry, and eggs. Tolerances are established for combined residues of the herbicide propanil and its metabolites (calculated as propanil) in

or on barley, oats, rice, wheat, milk, meat, eggs, and poultry at levels ranging from 0.05 ppm to 75 ppm (40CFR§180.274). There are no established Codex MRLs for propanil.

The available data bases for propanil consist of crop field trial data and FDA monitoring data. A Quantitative Usage Analysis for propanil was prepared by BEAD (David Donaldson; dated 2/21/01) and shows the maximum percent crop treated (%CT) with propanil is 88% on rice with a weighted average of 70%. Maximum %CT with propanil on barely, oat, and wheat is 1% or less.

The HED Dietary Exposure Evaluation Model (DEEM) is used to assess the risk from acute and chronic dietary exposure to propanil residues in food. The degree of refinement of the chronic DEEM analysis will be Tier 3, using FDA monitoring data for grains; highest average field trial (HAFT) residues to calculate residues in meat, milk, poultry and eggs; processing factors; and, incorporation of the percent of crop treated estimates and processing data. Although Tier 3, the risk assessment is considered upper-bound due to the use of upper-bound residues when estimating the dietary "burden" for livestock.

The Committee recognizes that further refinement to the dietary food exposure analyses may be required as the risk assessment is developed. Therefore, provided the final dietary food exposure assessment includes all metabolic residues of concern and does not underestimate the potential risk for infants and children, the safety factor recommendations of this Committee stand.

2. Dietary (Drinking Water) Exposure Considerations
(*Correspondence:* R. Griffin to B. Tarplee dated 09/06/01; Responses prepared by I. Abdel-Saheb)

The environmental fate database is complete for propanil. Available data indicate that propanil will not persist in the environment and is in the medium mobility class for sand, sandy loam, and clay loam soils. Based on mobility criteria detailed above, propanil would likely reach groundwater but due to its rapid metabolism in a water/soil matrix, it is not likely to persist for a significant amount of time to leach in measurable quantities. The possible exception are sites of extreme vulnerability and low metabolic capacity which would most probably occur only for terrestrial uses. The major degradate of propanil is 3,4 dichloroaniline and the HED MARC concluded that the residues of concern for drinking water risk assessment are propanil and residues convertible to3,4-DCA.

Available monitoring data include:

> Surface Water The USGS reported that for 62 agricultural streams sampled as part of NAWQA studies (1992-1996) by its National Water-Quality Assessment (NAWQA) program, that propanil was detected in only 2.56% of the 1560 water samples analyzed with a maximum concentration of 2.05 ppb. The frequency of sampling and the length of sampling period were not sufficient temporally and spatially to estimate potential drinking water concentrations for regulatory

purposes. Therefore, the ambient and drinking water assessments are based on the environmental models described below.

3,4-DCA is a common degradate for propanil, diuron, and linuron. A USGS study which analyzed 346 water samples collected in MS, MO, TN, AR, and North LA (mostly creeks, bayous and rivers) from February 1996-February 2001 (sampling every 2 weeks to one month) showed that 3,4-DCA did not exceed 26 ppb in surface water (96.2% detection rate, 333 detections, 13 non-detections) (Harris, 2001). Overall concentrations ranged from below the detection limit of 0.05 ppb to 26 ppb, with the majority of the sample detections being <1 ppb.

Ground Water EFED has limited monitoring data on the concentrations of propanil in groundwater. Even though the groundwater monitoring data collected by USGS (NAWQA) are from sites considered to be typical use areas, the frequency of sampling and the length of sampling period were not sufficient temporally and spatially to determine drinking water concentrations for regulatory purposes. Validated monitoring data for propanil for the states of California, Arkansas, Missouri, and Mississippi show that propanil was detected only in two wells out of a total of 124 in Missouri. The detected concentrations were 0.06 and 0.07 ppb.

In addition, the US Geological Survey (USGS) National Water Quality Assessment Program (NAWQA) analyzed pesticide occurrence and concentrations for major aquifers and shallow ground water in agricultural areas. Analysis of 933 samples (major aquifers study) showed propanil in 21% of the samples analyzed with concentrations below the detection limit (0.05 ppb). Maximum propanil concentration in 301 samples from shallow groundwater sites was 0.008 ppb.

The major component of the sampling design in the NAWQA study was to target specific watersheds and shallow ground water areas that are influenced primarily by a single dominant land use (agricultural or urban) that is important in the particular area. The ground-water data were primarily collected from a combination of production and monitoring wells. 45 Ground-water sites in the ground-water data were sampled for pesticides from a single snap-shot in time.

Screening models were used to determine estimated concentrations of propanil in groundwater and surface water. The SCI-GROW screening model was used to calculate potential ground water concentrations. It is based on a regression approach which relates the concentrations found in ground water in prospective ground water studies to aerobic soil metabolism rate and soil-water partitioning properties of the chemical.

The Environmental Fate and Effects Division does not have an officially approved model to predict concentrations of pesticides in rice paddy water. The approach taken here was based on a hypothetical rice paddy, 1 hectare in size, flooded to a depth of 10 cm, with a sediment interaction zone of 1cm. This screening calculation method models drinking water concentrations for the primary rice growing regions (California, Gulf Coast, and Mississippi Valley). The peak DW concentration is the concentration in the paddy on the day of release divided by two, since the volume of the reservoir and the volume of the paddies are roughly equal. A chronic concentration was obtained by decaying the peak concentration for a year at the aerobic aquatic rate, and taking the average over 365 days.

The FQPA SFCommittee recognizes that further refinement to the dietary water exposure analyses may be required as the risk assessment is developed. Therefore, provided the final dietary water exposure assessment does not underestimate the potential risk for infants and children and is inclusive of all degradates of toxicological concern, the safety factor recommendations of this Committee stand.

3. Residential Exposure Considerations
(*Correspondence:* R. Griffin to B. Tarplee dated 09/06/01)

There are no current registrations for use of propanil in a residential environment or on golf courses and other recreational areas. The current label for turf use will be worded to restrict use to sod farms *only*.

III. SAFETY FACTOR RECOMMENDATION AND RATIONALE

1. FQPA Safety Factor Recommendation

The Committee recommended that the FQPA safety factor for protection of infants and children (as required by FQPA) should be **retained at 10x** for propanil.

2. Rationale for Retaining the FQPA Safety Factor

The FQPA SFC concluded that the FQPA safety factor be **retained** at 10x for the following weight-of-evidence considerations:

- < there is qualitative evidence of increased susceptibility following pre- and postnatal exposure to propanil in the 2-generation reproduction study in rats;
- < a developmental neurotoxicity study with propanil is triggered due to suggestive evidence of neurotoxicity in the data base including neuropathological lesions (sciatic nerve degeneration) in a rat chronic/carcinogenicity study; and
- < there is also evidence consistent with neuro-endocrine disruption in the two-generation reproduction study in rats and in the rat chronic/carcinogenicity study. This evidence is supported by the Structure Activity Relationship (SAR) consideration that linuron, which is structurally related to propanil, has a known neuro-endocrine mode of action.

3. Application of the Safety Factor - Population Subgroups / Risk Assessment Scenarios

The safety factor is required for **All Population Subgroups** when assessing **Acute and Chronic Dietary Exposure and Residential Exposures of All Durations** due to the weight of the evidence stated above.